

5 As used herein, the phrase "modulate production of a
secondary metabolite" refers to a positive or negative or
desirable change in one or more of the variables or values
that affect the process or results of production of the
primary or secondary metabolites in a liquid or solid
10 state fungal fermentation. These positive or negative or
desirable changes include, without limitation, an increase
or decrease in the amount of a primary or secondary
metabolite being produced (in absolute terms or in
quantity per unit volume of fermentation broth or per unit
15 mass of solid substrate); a decrease in the volume of the
broth or the mass/quantity of substrate required for the
production of sufficient quantities; a decrease in the
cost of raw materials and energy, the time of fermentor or
culture run, or the amount of waste that must be processed
20 after a fermentor run; an increase or decrease in the
specific production of the desired metabolite (both in
total amounts and as a fraction of all metabolites and
side products made by the fungus); an increase or decrease
in the percent of the produced secondary metabolite that
25 can be recovered from the fermentation broth or culture;
and an increase in the resistance of an organism producing
a primary or secondary metabolite to possible deleterious
effects of contact with the secondary metabolite.

In certain embodiments of aspects of the invention, a
30 secondary metabolite is an anti-bacterial. An "anti-
bacterial" is a molecule that has cytocidal or cytostatic
activity against some or all bacteria. Preferred anti-
bacterials include, without limitation, β -lactams.

Preferred β -lactams include, without limitation,
35 penicillins and cephalosporins and biosynthetic
intermediates thereof. Preferred penicillins and
biosynthetic intermediates include, without limitation,
isopenicillin N, 6-aminopenicillanic acid (6-APA),
penicillin G, penicillin N, and penicillin V. Preferred
40 cephalosporins and biosynthetic intermediates include,
without limitation, deacetoxycephalosporin V (DAOC V),
deacetoxycephalosporin C (DAOC), deacetylcephalosporin C

5 (DAC), 7-aminodeacetoxycephalosporanic acid (7-ADCA),
cephalosporin C, 7-B-(5-carboxy-5-oxopentanamido)-
cephalosporanic acid (keto-AD-7ACA), 7-B-(4-
carboxybutanamido)-cephalosporanic acid (GL-7ACA), and 7-
aminocephalosporanic acid (7ACA).

10 In certain embodiments of aspects of the invention,
the secondary metabolite is an anti-hypercholesterolemic
or a biosynthetic intermediate thereof. An "anti-
hypercholesterolemic" is a drug administered to a patient
diagnosed with elevated cholesterol levels for the purpose
15 of lowering the cholesterol levels. Preferred anti-
hypercholesterolemic include, without limitation,
lovastatin, mevastatin, simvastatin, and pravastatin.

According to other embodiments of the invention, a
secondary metabolite is an immunosuppressant or a
20 biosynthetic intermediate thereof. An "immunosuppressant"
is a molecule that reduces or eliminates an immune
response in a host when the host is challenged with an
immunogenic molecule, including immunogenic molecules
present on transplanted organs, tissues or cells.
25 Preferred immunosuppressants include, without limitation,
members of the cyclosporin family and beauverolide L.
Preferred cyclosporins include, without limitation,
cyclosporin A and cyclosporin C.

In certain embodiments of aspects of the invention,
30 the secondary metabolite is an ergot alkaloid or a
biosynthetic intermediate thereof. An "ergot alkaloid" is
a member of a large family of alkaloid compounds that are
most often produced in the sclerotia of fungi of the genus
Claviceps. An "alkaloid" is a small molecule that
35 contains nitrogen and has basic pH characteristics. The
classes of ergot alkaloids include clavine alkaloids,
lysergic acids, lysergic acid amides, and ergot peptide
alkaloids. Preferred ergot alkaloids include, without
limitation, ergotamine, ergosine, ergocristine,
40 ergocryptine, ergocornine, ergotaminine, ergosinine,
ergocristinine, ergocryptinine, ergocorninine, ergonovine,
ergometrinine, and ergoclavine.

5 In certain embodiments of aspects of the invention,
the secondary metabolite is an inhibitor of angiogenesis
or a biosynthetic intermediate thereof. An "angiogenesis
inhibitor" is a molecule that decreases or prevents the
formation of new blood vessels. Angiogenesis inhibitors
10 have proven effective in the treatment of several human
diseases including, without limitation, cancer, rheumatoid
arthritis, and diabetic retinopathy. Preferred inhibitors
of angiogenesis include, without limitation, fumagillin
and ovalicin.

15 In certain embodiments of aspects of the invention,
the secondary metabolite is a glucan synthase inhibitor or
a biosynthetic intermediate thereof. A "glucan synthase
inhibitor" is a molecule that decreases or inhibits the
production of 1,3- β -D-glucan, a structural polymer of
20 fungal cell walls. Glucan synthase inhibitors are a class
of antifungal agents. Preferred glucan synthase
inhibitors include, without limitation, echinocandin B,
pneumocandin B, aculeacin A, and papulacandin.

 In certain embodiments of aspects of the invention,
25 the secondary metabolite is a member of the gliotoxin
family of compounds or a biosynthetic intermediate
thereof. The "gliotoxin family of compounds" are related
molecules of the epipolythiodioxopiperazine class.
Gliotoxins display diverse biological activities,
30 including, without limitation, antimicrobial, antifungal,
antiviral, and immunomodulating activities. Preferred
members of the "gliotoxin family of compounds" include,
without limitation, gliotoxin and aspirochlorine.

 In certain embodiments of aspects of the invention,
35 the secondary metabolite is a fungal toxin or a
biosynthetic intermediate thereof. A "fungal toxin" is a
compound that causes a pathological condition in a host,
either plant or animal. Fungal toxins could be mycotoxins
present in food products, toxins produced by
40 phytopathogens, toxins from poisonous mushrooms, or toxins
produced by zoopathogens. Preferred fungal toxins
include, without limitation, aflatoxins, patulin,